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Fig. 1

Figure 1: Fig. 1

Fig. 2

Figure 2: Fig. 2

Abstract

Full Text

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KINETICS OF THE AUTOOXIDATION OF PROPYL GALLATE IN AQUEOUS SOLUTION

The study of the kinetic regularities of the autooxidation of the normal propyl ester of gallic acid (PG) in aqueous solutions is of interest because this inhibitor of radical processes is capable of retarding the development of tumor processes and of exerting a protective effect against radiation injury ([1–4]). These data have also been confirmed in other works ([5–9]). It has been established that in some cases the biological effect is connected not with the original structure itself, but with free radicals arising from the inhibitor in the course of its oxidation ([10,11]). A considerable number of studies has been devoted to the autooxidation of pyrogallol and its derivatives, among which PG may be included. However, these works contain mainly data on the identification of molecular intermediate oxidation products ([12–14]). The kinetic regularities of the process are not considered in them.

In the present work the course of the oxidation process of PG was followed by the decrease in the concentration of PG, determined polarographically. The determination was carried out in borate buffer at pH 7.2–7.4 relative to an external saturated calomel electrode immersed in $0.1M$ KCl. It was shown that the half-wave potential ($\pi/2$) of PG depends linearly on the pH of the medium in the pH interval from 7.1 to 8.6, which agrees with literature data for the determination of PG in acetate buffer at pH 4.3–7.38 ([15]). Since a strong dependence of the wave height on temperature was found (on going from 10 to 25° the wave height increases by a factor of 6.4), all measurements were carried out in a thermostatted cuvette at 21°. In the presence of oxidation products amounting to up to 40% of the initial amount of inhibitor, PG is determined with an accuracy of $\pm 1.5\%$.

Fig. 1

Fig. 2

Using the polarographic method, it was possible to follow the kinetic regularities of the oxidation of PG by molecular oxygen in borate buffer at pH 7.0-9.0 and at temperatures of 33-80°. Oxygen was supplied through a capillary tube at a rate of 1.7 liters/hour. In special experiments it was shown that under these conditions the reaction rate does not depend on the rate and

method of oxygen supply (through a capillary tube or through a porous plate). From the kinetic curves of PG oxidation shown in Fig. 1, it is evident that the oxidation rate increases with increasing alkalinity of the medium. The dependence of the oxidation rate on the pH of the medium is also clearly manifested in experiments in which the pH of the medium is changed during oxidation. As can be seen from Fig. 2, oxidation practically ceased when, 27 min after the start of the experiment, the pH of the medium was changed from 8.6 to 7.4. These results indicate that only ionized PG molecules enter into the reaction. The dependence of the oxidation rate on the pH of the medium in the coordinates $\lg W$—pH gives a straight line with a slope equal to unity. This means that the reaction rate is proportional to the concentration of OH^- ions to the first power and that singly charged PG ions enter into the reaction.

Fig. 3 Fig. 4

Fig. 3 **Fig. 4**

Figure 3 shows the dependence of the logarithm of the reaction rate on the logarithm of the PG concentration. The straight line obtained in these coordinates, drawn by the least-squares method, has a slope equal to 1 ± 0.1, i.e., the reaction is first order with respect to the initial PG concentration. At the same time, as can be seen from Fig. 1, PG is oxidized at a constant rate at least up to 50% conversion (oxidation to greater depths was not studied by us), i.e., the reaction is zero order with respect to the current PG concentration.

The zero order of the reaction can apparently be explained by the catalytic action of the quinone formed in the course of oxidation. The phenomenon of catalysis of the oxidation reaction by quinone has been studied in detail for methyl derivatives of hydroquinone^(16-18). It is quite possible that the decrease in the reaction rate due to consumption of the initial PG is compensated by the interaction of quinone with PG with formation of semiquinone. The rate of the latter reaction must increase during the course of oxidation, since otherwise a constant rate of PG consumption would not be observed. This, in turn, means that the quinone concentration must increase during oxidation. At the same time, the rate of interaction of quinone with the initial phenol may be very high, as follows from literature data, and therefore the quinone concentration throughout the entire course of oxidation may remain very low and, consequently, difficult to determine analytically.

The dependence of the oxidation rate on temperature was studied at two pH values: 7.6 and 8.8. The data obtained in the coordinates $\lg W - 1/T$ (Fig. 4) give parallel straight lines, from the slope of which an activation energy value of $18\,000 \pm 700$ cal/mol was obtained.

It is stated in the literature^(19) that the limiting stage of the oxidative transformations of polyphenols is the stage of semiquinone formation. It may therefore be assumed that the activation energy measured by us

corresponds to the activation energy of the oxidation process of the ionized molecule in semiquinone. Since, when the pH of the medium is varied, the magnitude of the activation energy does not change, this indicates that throughout the investigated range of pH values the rate-limiting step is the same elementary stage.

In a polarographic study of oxidized PG in borate buffer at pH 7.2, in the cathodic region a distinct wave was found with $\pi/2$ equal to 1.17 V. In the oxidation products one might have expected the presence of hydrogen peroxide, an oxy-orthoquinone, or products of deeper oxidation. In a separate experiment it was shown that H_2O_2 under the same conditions gives a wave with $\pi/2 =$ 1.2 V. Likewise, addition of H_2O_2 at a concentration of $2.7 \cdot 10^{-4} M$ to the polarographed sample leads to an increase of the wave with $\pi/2 = 1.17$ V. Thus, the observed wave at $\pi/2 = -1.17$ V should be attributed to the presence of hydrogen peroxide in the reaction products. The formation of H_2O_2 during the oxidation of PG was also confirmed by a qualitative reaction for H_2O_2 with $(TiO_2 + H_2SO_4)$. The slight shift of $\pi/2$ for H_2O_2 in the oxidate is apparently caused by the presence in the sample of other oxidation products. On the basis of literature data and our experimental data, the following scheme may be proposed for the oxidation of PG in aqueous solutions.

$$C_6H_2(OH)_3COOC_3H_7 + OH^- \rightleftharpoons C_6H_2(OH)_2(O^-)COOC_3H_7 + H_2O \quad (1)$$

$$C_6H_2(OH)_2(O^-)COOC_3H_7 + O_2 + OH^- \rightleftharpoons C_6H_2(OH)(O^\bullet)(O^-)COOC_3H_7 + H_2O + O_2^{\bullet -} \quad (2)$$

$$C_6H_2(OH)(O^\bullet)(O^-)COOC_3H_7 + O_2 \rightleftharpoons C_6H_2(OH)(=O)(O)COOC_3H_7 + O_2^{\bullet -} \quad (3)$$

$$C_6H_2(OH)(=O)(O)COOC_3H_7 + C_6H_2(OH)_2(O^-)COOC_3H_7 + OH^- \rightleftharpoons 2\,C_6H_2(OH)(O^\bullet)(O^-)COOC_3H_7 + H_2C \quad (4)$$

$$C_6H_2(OH)(=O)(O)COOC_3H_7 + O_2 \longrightarrow \text{humic acids} \quad (5)$$

$$[\text{structural formula}] + O_2^- + H_3O^+ \rightarrow [\text{structural formula}] + H_2O_2 + H_2O. \quad (6)$$

$$[\text{structural formula}] + O_2^- + 2H_3O^+ \rightarrow [\text{structural formula}] + H_2O_2 + 2H_2O. \quad (7)$$

The presence of free-radical intermediates in the reaction mechanism makes it possible, from these positions, to explain the diverse effects observed when phenolic inhibitors are used in experimental biology. The authors express their gratitude to L. I. Solov' eva for assistance in the experiment.

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Note: Figure translations are in progress. See original paper for figures.